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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/618,126  | 07/11/2003  | Wayne A. Froland     | MSB 7295            | 6003             |
| 35969   | 7590        | 10/04/2006           | EXAMINER            |                  |
| JEFFREY M. GREENMAN<br>BAYER PHARMACEUTICALS CORPORATION<br>400 MORGAN LANE<br>WEST HAVEN, CT 06516 |             |                      | PAK, MICHAEL D      |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1646                |                  |

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/618,126             | FROLAND ET AL.      |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Michael Pak            | 1646                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above claim(s) 2-7, 9-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's election of Group I, claims 1, 7 and 8, species SEQ ID NO:115 in the reply filed on July 14, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 1 and 8 are examined. Claims 2-7 and 9-53 are withdrawn as non-elected invention.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims encompass non-elected invention which is ambiguous.

4. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 1 encompasses a using polypeptide variants, derivatives and fragments of SEQ ID NO:115 without structural and functional limitations. However, the essential feature of the invention is SEQ ID NO:115, and one of skilled in the art cannot envision the full genus of molecules of the claimed polypeptide molecules. The claims encompass variants and derivatives whose structure is not known or other variant proteins with different function from SEQ ID NO:115 taught in the specification. Claimed protein variants and derivatives encompass a large genus of proteins which are alleles or variants whose function has yet to be identified from different species of animal because the structure of the newly identified naturally occurring protein is not known. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the specification.

5. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising SEQ ID NO:115, does not reasonably provide enablement for a polypeptide variant, derivative or fragments without structural and functional limitation. The specification does not enable any

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person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of § 112 requires that the patent specification enable "those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." Genentech, Inc. v. Novo Nordisk AIS, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)); see also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Likewise, in Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), the court affirmed the holding of invalidity of claims to analogs of the EPO gene under § 112 for lack of enablement where applicants had

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claimed every possible analog of the EPO gene but had disclosed only how to make EPO and a very few analogs. "[D]espite extensive statements in the specification concerning all analogs of the EPO gene that can be made, there is little enabling disclosure of the particular analogs and how to make them .... There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." *Id.*, 927 F.2d at 1213-14, 18 USPQ2d at 1027.

Claims encompass variants, derivatives and fragments with unlimited changes to SEQ ID NO:115. However, one skilled in the art cannot make and use variants, derivatives and fragments of SEQ ID NO:115. The amount of direction provided in the specification is limited to a specific species of SEQ ID NO:115. One skilled in the art would require empirical experimentation in order to determine the changes to SEQ ID NO:115 sequence without disrupting the structure for the protein activity. However, the specification does not teach how to use variants, derivatives and fragments of SEQ ID NO:115 which are functional. PACAP have active sites which are essential for the proper function of the protein in its interaction with the the polypeptide agonist domains (Pan et al., US 6,972,319). A fragment of the polypeptide which is truncated in the middle of the various domains or a fragment which does not allow the proper folding of the domain or is deleted would not be expected to function. The state of the art is such that one skilled in the art cannot predict the outcome of changes to protein structure using the primary amino acid structure as the predictor (Bowie et al., Science, 1989). Thus, one skilled in the art cannot use the primary amino acid sequence of SEQ ID

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NO:115 polypeptide alone to predict the tertiary structure of SEQ ID NO:115 polypeptide which would be required to determine the PACAP function and proper folding of SEQ ID NO:115 polypeptide. No working example is provided to determine whether a change in the domains of SEQ ID NO:115 polypeptide fragment or variant would provide proper function. It would require empirical experimentation to determine whether the variants of SEQ ID NO:115 is functional. Thus, such fragments and variants encompass a genus with a large number of species which are not functional. In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not make the invention without undue experimentation. Therefore, based on the above Wands analysis, a preponderance of the evidence supports a conclusion that one skilled in the art would not have been enabled to make and use the claimed invention without undue experimentation.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Pan et al. (US 6,972,319).

Pan et al. disclose many peptides (SEQ ID NO: 72, 174, 75) which is 89% identical in amino acid sequence to the claimed SEQ ID NO:115. Pan et al. polypeptide

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meets the limitation of the term claimed because no structure is claimed and encompasses the term variants, derivatives and fragments.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:30 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Michael Pak



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Primary Patent Examiner

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26 September 2006